

Appl. Serial No. 09/675,323
Amdt. dated Dec. 2, 2003
Reply to Office action of June. 6, 2003

PATENT

REMARKS AND RESPONSE TO OFFICE ACTION

After entry of this paper claims 33-55 are pending. Claims 53-55 are new. The disclosure supports the amendments, which add no new matter. Support for the new claims is found throughout the disclosure with exemplary support as follows. Support for new claims 53-55 is at least at pages 38-55, and original claims 2-4.

Informalities

The Office objected to the disclosure as missing figures that the application refers to and a brief description of the figures section. Applicants have amended the specification to remove reference to figures in examples 2-5. These amendments obviate the need for a brief description of the figures section. In view of these amendments, Applicants respectfully request withdrawal of the objection.

35 U.S.C. § 112, first paragraph

The Office objected to the specification and rejected claims 40-52 as allegedly not enabled. The Office stated that the claims are enabled for treatment of breast cancer and prostate cancer for exemplified compounds 0-22. However the Office objected to the specification and maintained the prior rejection of the claims as allegedly lacking sufficient enablement for treating other claimed diseases and for not being capable of preventing any claimed disease condition. For reasons described below, Applicants respectfully traverse the rejection.

To establish and maintain a rejection under 35 U.S.C. §112, first paragraph, the Office must provide logical reasoning to support its position. The Office must "explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi and Horton*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971). The Office must advance "substantive reasons why the instant specification is non-

Appl. Serial No. 09/675,322
Amdt. dated Dec. 2, 2003
Reply to Office action of June. 6, 2003

PATENT

enabling." "Mere broad generalizations and allegations are insufficient for holding of non-enablement." *Ex parte Goeddel* 5 U.S.P.Q. 2d 1449 (B.P.A.I. 1987). The first paragraph of 35 U.S.C. § 112 requires nothing more than objective enablement. *In Re Vaeck* 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991), *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.* 224 U.S.P.Q. 409 (Fed. Cir. 1984). It is irrelevant whether objective enablement is based on working examples or on broad terminology. *In Re Vaeck*, supra, *Atlas Powder Co.*, supra. To meet the requirement under the first paragraph of § 112, the specification, when filed, must enable one skilled in the particular art to use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). In addition, even if some of the claimed embodiments were inoperative, the claims are not necessarily invalid. "It is not a function of the claims to specifically exclude . . . possible inoperative substances . . ." *Atlas Powder Co.*, supra, *In re Dinh-Nguyen*, 492 F.2d 856, 858-59 (C.C.P.A. 1974). As explained below, Applicants respectfully submit that the claims are fully enabled as described below.

To support the rejection, the Office asserted that no known method existed to prevent any androgen related disease in any healthy patient. However, methods for treating and preventing androgen related disease conditions have been described. For example, claim 27 of U.S. patent 6,642,227 (issued November 4, 2003) newly cited, claims a method to treat or prevent angiogenic disorders including solid tumors. Solid tumors include not only prostate cancer and breast cancer, but many other tumor types as well. Similarly, claim 3 of U.S. patent 4,005,194 (issued January 25, 1977), newly cited, claims a method to reduce or prevent prostatic hyperplasia, a condition that some of the present claims recite. U.S. patent 4,310,523 (of record), discussed under the rejection under § 102(b) below, recites a method to prevent or treat prostatic hyperplasia. Recently published clinical study results (I.M. Thompson et al., *New Engl. J. Med.* 349:215-224 2003, newly cited) indicate that treating healthy patients prevents prostate cancer. Clearly, methods to prevent androgen-responsive

Appl. Serial No. 09/675,323
Amdt. dated Dec. 2, 2003
Reply to Office action of June. 6, 2003

PATENT

diseases are known. Applicants respectfully submit that, in view of the cited references, this basis for the Office's rejection is incorrect.

The Office alleged that since data for "only 23" compounds was contained in the application, the scope of the claims was not enabled. The Office asserted
5 that compounds 0-22, which are exemplified in the specification, are enabled for treating prostate and breast cancer. However, the Office alleged that this evidence is insufficient to support the scope of the claims. As noted above, satisfying the enablement requirement does not require that every possible embodiment be exemplified by working examples. *In Re Vaeck*, supra. The
10 Office alleges that undue experimentation would be needed to practice the invention because there is insufficient teaching in the specification. The Office noted that the specification did not contain data for compounds where R⁵ or R⁶ are moieties such as an oligosaccharide. The Office alleged that the invention has an unpredictable nature, but provided no rationale about why the invention
15 was unpredictable. Also, the Office did not provide any reasoning why the mentioned compounds would be expected to be inactive. Applicants respectfully traverse the rejection.

To practice the claimed invention, one of ordinary skill in the art would use the guidance in the application to to practice the claimed methods. Applicants To
20 practice the claimed methods, teaching of dosages and routes of administration in the specification, e.g., at pages 30 and 31, would have been used. If desired, the biological activity of the compounds could have been characterized in a manner such as that described in the specification, e.g., at pages 79-81. Applicants have provided the objective evidence of enablement that the law
25 requires. *In Re Vaeck*, supra, *Atlas Powder Co.*, supra. The law is clear that enablement is not precluded by the use of routine screening: "That some experimentation is necessary does not preclude enablement, the amount of experimentation, however, must not be unduly extensive." *Atlas Powder Co.*, supra. At most, one of ordinary skill in the art would employ routine
30 experimentation to practice the claimed methods.

Appl. Serial No. 09/675,320
Amdt. dated Dec. 2, 2003
Reply to Office action of June. 6, 2003

PATENT

To respond to specific concerns that the Office may have, Applicants need a more detailed rationale of why the claims are allegedly not enabled. As noted above, an assertion that not all classes of compounds are exemplified is an insufficient basis on which Applicants can respond. Particularized reasoning by the Office is needed, *Ex parte Goeddel*, supra, *In re Marzocchi and Horton*, supra, which would provide Applicants specific points on which to respond.

Applicants note that the disclosure in the present application related to enablement is commensurate with similar disclosure in other U.S. patents. The Office's attention is directed, for example, to U.S. patent 6,642,227 (hereafter the '227 patent) newly cited, described above. A rough estimate of the number of compounds that the claimed treatment methods in the '227 patent include is in excess of about 10^{10} compounds. Despite the broad range of chemical structures, claims 1 and 19 cover any tumor or cancer as a 'proliferative disease' and claim 27 recites treating or preventing solid tumors with the same scope of compounds and, in view of the other claims, many other diseases. This situation exists despite the disclosure in '227, which states that some of the target molecules are possible targets for therapeutic intervention, e.g., col. 3 at lines 17-24 states that Src kinases are 'potential' therapeutic targets. Thus, in the '227 patent, a limited number of compound structures are exemplified in the specification, while claim 1 is not similarly limited to those structures. By contrast with the '227 patent, the present application describes a well-defined group of clinical indications.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection.

35 U.S.C. § 112, second paragraph

The Office rejected claims 40-52 as being indefinite, since they depended on non-elected claims. The Office also noted that withdrawn claims 34-38 lacked proper antecedent basis for R^5 or R^6 being hydrogen. The present amendments have corrected the claims to eliminate their dependency on non-elected claims

Appl. Serial No. 09/675,323
Amdt. dated Dec. 2, 2003
Reply to Office action of June. 6, 2003

PATENT

and to provide the proper antecedent basis. Applicants request withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, in view of the amendments to the claims.

5

35 U.S.C. § 102(b) or 103(a)

The Office rejected claims 40-52 as being anticipated by, or obvious in view of, International patent publication No. WO 97/37662 or U.S. patent No. 4,310,523 (hereafter the '523 patent), both of record.

To anticipate under 35 U.S.C. § 102, a reference must disclose each
10 element and limitation of the claims and that this was known or used by others before it was invented by the applicant. A single reference must describe the claimed invention with sufficient precision and detail to establish that the subject matter existed in the prior art. See, e.g., *Hoover Group, Inc. v. Custom Metalcraft, Inc.*, 66 F.3d 299, 302, 36 U.S.P.Q.2d 1101, 1103 (Fed. Cir. 1995), *In re Spada*, 911 F.2d 705, 708, 15 U.S.P.Q.2d 1655, 1657 (Fed. Cir. 1990). The
15 prior knowledge by others requires that all of the elements and limitations of the claimed subject matter must be expressly or inherently described in a single prior art reference. *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1950 (Fed. Cir. 1999), *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560,
20 1571, 7 U.S.P.Q.2d 1057, 1064 (Fed. Cir. 1988).

To establish a case of prima facie obviousness, the Office must identify specifically the principle known to one of ordinary skill in the art that suggests the claimed combination, even if the level of skill is high, *In re Rouffet* 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998), or make particular findings as to why one of ordinary skill
25 in the art without knowledge of the claimed invention would have selected the components for combination in the manner claimed (*In re Kotzab* 55 PQ2d 1313 2000), *In re Sang Su Lee* 277 F.3d 1338, 1345-46, 61 USPQ2d 1430, 1435 (Fed. Cir. 2002). Thus, to maintain a case of prima facie obviousness, the Office must show that the cited references contain a teaching or suggestion or motivation to
30 combine the references. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352,

Appl. Serial No. 09/675,323
Amdt. dated Dec. 2, 2003
Reply to Office action of June. 6, 2003

PATENT

48 U.S.P.Q.2d 1225, 1232 (Fed. Cir. 1998). This requires a showing of specific reasons one of ordinary skill in the art would have been motivated to select the references and combine them. *In re Rouffet*, 149 F.3d 1350, 1359, 47 U.S.P.Q.2d 1453, 1459 (Fed. Cir. 1998). To avoid a rejection based on hindsight, evidence of teaching or suggestion to combine references is necessary. *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988).

The amended claims require the presence of a carbonate (-O-C(O)-OR) at the 3-position and have an optional double bond at the 1-2 and/or 5-6 positions. The WO 97/37662 publication discloses compounds that have a double bond at the 5-6 position and that can have an ether or ester at the 3-position, but no carbonate structure. The steroid compounds in the '523 patent require the presence of a double bond at both the 4-5 and 6-7 positions. Thus the compounds in the cited references do not expressly or inherently contain the presence of any carbonate moiety at the 3-position. Because of this, the references do not contain each element that is claimed and they can not support the rejection under § 102(b). *In re Robertson*, supra, *Constant v. Advanced Micro-Devices, Inc.*, supra. Applicants request reconsideration and withdrawal of the § 102(b) rejection.

Regarding the § 103(a) rejection, Applicants note that the amended claims differ structurally from the cited references. As noted above, the amended claims require the presence of a carbonate moiety at the 3-position. The structure differences between compounds in the cited references and the claims do not render the claimed methods obvious under § 103(a). The cited references do not contain or provide a rationale or reasoning to support modifying the structures in the cited references to arrive at the presently claimed structures. Such reasoning is needed to support a § 103(a) rejection. *In re Rouffet*, supra, *In re Sang Su Lee*, supra. In view of this, Applicants respectfully request reconsideration and withdrawal of the § 103(a) rejection.

30

Appl. Serial No. 09/675,323
Amdt. dated Dec. 2, 2003
Reply to Office action of June. 6, 2003

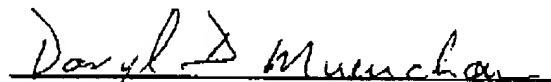
PATENT

OTHER MATTERS

Applicants direct the Office's attention to related, copending application serial Nos. 09/535,675, 09/820,483, 10/087,929, 10/319,356, 10/329,065, 10/602,330, 10/606,524, 10/607,035 and 10/607,415, which are cited in the information disclosure statement that accompanies this paper.

Applicants believe that amended claims are allowable and reconsideration and withdrawal of the rejections is respectfully requested. Applicants' representative can be reached at the number given below if the Office has any questions or would like to address any other matters that may arise.

Respectfully submitted,

Dated: 12-3-03

Daryl D. Muenchau, Reg. No. 36,616
Hollis-Eden Pharmaceuticals, Inc.
4435 Eastgate Mall, Suite 400
San Diego, CA 92121
Phone: 858-320-2569
Fax: 858-558-6470